

SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of safety and effectiveness is being submitted in accordance with the requirements of The Safe Medical Devices Act of 1990 (SMDA 1990) and 21 CFR 807.92.

I. GENERAL INFORMATION

Date of Summary Preparation:	August 28, 2002
Distributor:	BRAHMS Diagnostica LLC 35 B South Peachtree Street Norcross, Georgia 30071
Manufacturer:	BRAHMS AG Neuendorfstrasse 25 16761 Hennigsdorf/Berlin Germany
Contact Person:	William G. Frank BRAHMS Diagnostica LLC 35 B South Peachtree Street Norcross, Georgia 30071
Device Name:	DYNOtest Tg-pluS
Common or Usual Name:	Immunoradiometric assay for the quantitative determination of thyroglobulin in human serum
Classification:	ClassII
Regulation Number:	866.601
Product Code:	MSW, Immunology
Substantial Equivalence To:	Nichols Institute Diagnostics Chemiluminescence Thyroglobulin

II. INTENDED USE

DYNOtest Tg-pluS is a immunoradiometric assay (IRMA) for the quantitative determination of thyroglobulin in human serum. It is intended to aid in the monitoring for the presence of local or metastatic thyroid tissue in patients who have had thyroid gland ablation (by surgery with or without radioiodine therapy). DYNOtest Tg-pluS is also indicated for detecting the presence of thyroid tissue in patients with differentiated thyroid cancer when used with radioiodine whole body scans after recombinant thyrotropin (TSH) stimulation or thyroid hormone

withdrawal. DYNOfest Tg pluS includes a recovery test to aid in the detection of interfering anti-thyroglobulin antibodies or other substances.

III. DEVICE DESCRIPTION

DYNOfest Tg-pluS is a two-step immunoradiometric assay for the quantitative determination of thyroglobulin in human serum using a coated tube technique. Two antigen specific antibodies that recognize different binding sites on the antigen (thyroglobulin) are used in excess. In the first step, thyroglobulin in the sample, standard or control binds to rabbit anti-human Tg polyclonal antibodies attached to the solid phase. Following incubation, unbound thyroglobulin and serum components are washed from the tube. In the second step, the radioactive tracer (mouse anti-human thyroglobulin monoclonal antibody) reacts with the bound antigen forming a sandwich complex fixed to the side of the tube. Following a second incubation, unreacted tracer is washed from the tube and remaining radioactivity in the tubes is measured. The measured radioactivity is directly proportional to the quantity of thyroglobulin in the sample, standard or control. The standard curve is used to derive the thyroglobulin concentration in the patients samples.

Recovery Test: Because non-specific interferents and anti-thyroglobulin antibodies can result in falsely low thyroglobulin values, DYNOfest Tg-pluS includes a recovery test, the purpose of which is to aid in the detection of such interferences. In the recovery test, recovery buffer containing a known quantity of thyroglobulin, is added to the patient sample. In parallel, the recovery buffer is added to a recovery reference sample (thyroglobulin free serum). The patient sample, recovery sample and recovery reference sample are all run using DYNOfest Tg-pluS. The percentage recovery is determined by subtracting the patient Tg value from the patient recovery sample and dividing this result by the recovery reference Tg value:

$$\frac{\text{Recovery Tg} - \text{Patient Tg}}{\text{Recovery reference Tg}} \times 100 = \% \text{ Recovery}$$

Recovery values between 70% and 130% are considered valid. Values <70% and >130% are due to interferences; these patient results should be considered invalid.

IV. COMPARISON TO PREDICATE DEVICE

Comparison to predicate device: DYNOfest Tg-pluS is substantially equivalent to the Nichols Institute Diagnostics Chemiluminescent Thyroglobulin assay (K994140). The following method comparison study included 133 samples from patients diagnosed with thyroid cancer. Concordance testing yielded the following results:

NID Chemiluminescent Thyroglobulin

DYNOtest Tg-pluS	≤ 2.0 ng/mL	2.1-4.9 ng/mL	5.0-9.9 ng/mL	10.0-29.9 ng/mL	30.0-59.9 ng/mL	≥ 60.0 ng/mL
≤ 1.0 ng/mL	61	3	0	0	0	0
1.1-2.4 ng/mL	1	13	4	0	0	0
2.5-4.9 ng/mL	0	3	7	0	0	0
5.0-14.9 ng/mL	0	0	1	19	2	0
15.0-29.9 ng/mL	0	0	0	1	3	1
≥ 30.0 ng/mL	0	0	0	0	0	14

Note: DYNOtest Tg-pluS is calibrated against CRM 457 at a ratio of 0.5:1 whereas the comparison method is calibrated against CRM 457 at a 1:1 ratio

Agreement for results using 1.0 ng/mL determined with DYNOtest Tg-pluS as the cutoff compared to 2.0 ng/mL Tg as the cutoff for the comparison method = 96.9% (129/133).

The following tables outline the similarities and differences between the BRAHMS DYNOtest Tg-pluS assay and the Nichols Institute Diagnostics Chemiluminescent Thyroglobulin assay.

	DYNOtest® Tg-pluS	NID Chemiluminescent Tg
Analyte	Thyroglobulin	Thyroglobulin
Specimen	Serum	Serum
Intended Use	DYNOtest Tg-pluS is intended to aid in the monitoring for the presence of local and metastatic thyroid tissue in patients who have had thyroid gland ablation (using surgery with or without radioactivity). DYNOtest Tg-pluS is also indicated for detecting the presence of thyroid tissue in patients with differentiated thyroid cancer when used with radioiodine whole body scans after recombinant thyrotropin (TSH) stimulation or thyroid hormone withdrawal.	The NID Chemiluminescent Thyroglobulin assay is intended to aid in monitoring for the presence of local and metastatic thyroid tissue in patients who have had prior thyroidectomy (using surgery with or without radioiodine). The assay is also indicated for monitoring thyroglobulin levels in combination with radioiodine whole body scans after either rhTSH administration or thyroid hormone withdrawal for detecting presence of thyroid tissue in patients with well-differentiated thyroid cancer. The assay should only be used on patients who lack thyroglobulin autoantibodies.
Result	ng/mL	ng/mL

	DYNOtest® Tg-pluS	NID Chemiluminescent Tg
Format	Two-step immunometric assay that measures radiation from I 125 to determine results . Two antigen specific antibodies that recognize different binding sites on the thyroglobulin molecule are used in excess.	Immunometric assay that measures chemiluminescence to determine results. The assay uses a biotinylated goat antibody for capture and an acridinium-labeled mouse monoclonal antibody for detection.
Solid Phase	Polystyrene 12 x 75 mm tube	Avidin-coated bead
Reader	Gamma counter	Luminometer
Standard	CRM 457 – In the DYNOtest Tg-pluS assay 1.0 ng/mL Tg = 2.0 ng/mL CRM 457	CRM 457 – 1.0 ng/mL Tg = 1.0 ng/mL CRM 457
Incubation	Overnight	Overnight
Reportable Range	0 – 250 ng/mL	0 – 100 ng/mL
Sensitivity	Analytical = 0.08 ng/mL Functional = 0.1 ng/mL	Analytical = 0.07 ng/mL Functional = 0.5 ng/mL
Precision (Intra-Assay %CV)	% CV from 1.5 – 5.6% 5 samples from 0.4 – 55 ng/mL	% CV from 3.6 – 6.4% 6 samples from 1.1 – 94 ng/mL
Precision (Inter-Assay % CV)	% CV from 2.2 – 6.4% 5 samples from 0.4 – 55 ng/mL	% CV from 5.0 – 22% 6 samples from 0.4 – 36 ng/mL
Dilution Parallelism	N = 5; 93.9 – 99.6%	N = 5; 83 – 120%
Recovery	N = 5; 96.1 - 102%	N = 3; 94.1 – 107.5%
High Dose Hook	Up to 30,500 ng/mL	Up to 1,000 ng/mL
Controls	2	2

V. Clinical Performance

In a clinical study to evaluate the performance of DYNOtest Tg-pluS conducted at a single site, 133 patients diagnosed with thyroid cancer were assigned to one of three clinical categories: (1) patients believed free of normal and malignant thyroid tissue, n = 51; (2) patients with active metastatic disease, n = 35; and (3) patients with residual thyroid/thyroglossal duct remnants, n = 47. Assignment to each category was based on Tg results from a reference method (immunochemiluminescent method) combined with results from radioiodine whole body scans following TSH stimulation by administration of recombinant TSH or withdrawal of thyroid hormone therapy. All 133 patients had negative thyroid autoantibody results.

	Reference Methodology		
	Pos.	Neg	
DYNOtest Tg pluS	Pos.	64	5
	Neg	18	46
		82	51
			133

A cut-off value of ≥ 1.0 ng/mL was used to indicate those patients with suspect local or metastatic disease. When patients were assessed using the reference methods described, DYNOtest Tg-pluS demonstrated an overall clinical sensitivity of 78.1% (64/82) and a specificity of 90.2% (46/51). The positive predictive value was 92.8% (64/69) and the negative predictive value was 71.9% (46/64). The sensitivity of DYNOtest Tg pluS was

100% (35/35) in patients with active metastatic disease and 61.7% (29/47) in patients with residual thyroid/thyroglossal duct remnants. The specificity of DYNOfest Tg pluS in patients free of normal and malignant tissue was 90.2% (46/51).

Interference from Thyroglobulin auto-antibodies

In a separate study, interference from Tg auto-antibodies was tested in 77 sera that had tested positive for Tg auto antibodies using a radioimmunometric assay (DYNOfest anti-TGn), (minimum 65.2 kilounits/L; maximum, 8150 kilounits/L; median, 181 kilounits/L). Recovery (50 µg/L) was disturbed in the DYNOfest Tg pluS assay in seven sera (9%). Recovery was considered undisturbed if measured Tg values were 70 – 130% of the added Tg. Except for one serum sample, all sera with disturbed recoveries had Tg values <1µg/L and autoantibodies > 800 kilounits/L.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. William G. Frank
General Manager
BRAHMS Diagnostica, LLC
35 B South Peachtree Street
Norcross, Georgia 30071

SEP 17 2002

Re: k021057
Trade/Device Name: DYN0test Tg-pluS
Regulation Number: 21 CFR § 866.6010
Regulation Name: Tumor Associated Antigen Immunological Test System
Regulatory Class: II
Product Code: MSW
Dated: July 12, 2002
Received: July 18, 2002

Dear Mr. Frank:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

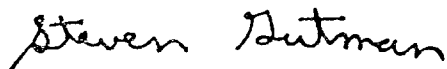
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive, slightly slanted style.

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

K 021057/A

1. Indications for Use Statement

510(k) Number (if known): K021057

Device Name: DYNOfest Tg-pluS

Indications For Use

DYNOfest Tg-pluS is a immunoradiometric assay (IRMA) for the quantitative determination of thyroglobulin in human serum. It is intended to aid in the monitoring for the presence of local or metastatic thyroid tissue in patients who have had thyroid gland ablation (by surgery with or without radioiodine therapy). DYNOfest Tg-pluS is also indicated for detecting the presence of thyroid tissue in patients with differentiated thyroid cancer when used with radioiodine whole body scans after recombinant thyrotropin (TSH) stimulation or thyroid hormone withdrawal. DYNOfest Tg-pluS includes a recovery test to aid in the detection of interfering anti-thyroglobulin antibodies or other substances.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE
IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ☒

OR

Over-The Counter ☐

Deborah M. Moore

(Division Sign-Off)

Division of Clinical Laboratory Devices

510(k) Number K021057

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